Wyeth v. Levine's 'Clear Evidence' Language: Clearly Misunderstood

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In 2009, the United States Supreme Court in Wyeth v. Levine affirmed a judgment rejecting a prescription drug manufacturer's contention that plaintiff's claim that the manufacturer should have strengthened its U.S. Food and Drug Administration-approved warnings was preempted by the Federal Food, Drug and Cosmetic Act (FDCA). The court noted it would not find preemption in that case "absent clear evidence that the FDA would not have approved a [warning] change" and held that the manufacturer had "offered no such evidence."[1]

Subsequently, many courts have interpreted Wyeth as holding both that the burden in such a case is on defendant to prove the FDA would have rejected the warning advocated by the plaintiff and that the standard is an "exacting" one beyond the normal preponderance-of-the-evidence standard. In fact, neither proposition is correct: the locus of the burden was never litigated in Wyeth, and its "clear evidence" language was necessitated by the fact that the preemption issue turned on factual findings made by the Vermont courts, which the Supreme Court could not ordinarily reverse absent exceptional circumstances.

Moreover, for many reasons the burden in a prescription drug failure-to-warn case such as Wyeth should be on the plaintiff to show the FDA would have approved the warning for which the plaintiff advocates, not on defendant to show the agency would have rejected it. For example, under traditional principles the burden of proof would fall on plaintiff regardless of whether the regulatory submission — and ultimate approval — of a warning change is characterized as an essential element of the plaintiff's claim, or as a regulatory exception relied on by the plaintiff to counter the statutory provision that would make defendant's use of an unapproved warning unlawful. In addition, minimizing the risk that state law will disturb the delicate balance of federal objectives struck by the FDA in finding a drug safe under its approved labeling — and not changing that position despite reviewing all adverse event reports from all manufacturers of drugs posing the same risk — at the very least requires that a plaintiff claiming the FDA would have approved a different warning bear the burden of proof.

A Proper Understanding of Wyeth

The plaintiff in Wyeth suffered gangrene and an arm amputation after a physician's assistant attempting an intravenous injection of the anti-migraine drug Phenergan inadvertently injected it into or near an artery. The defendant's FDA-approved labeling explicitly warned of this risk and cautioned that for this reason a gradual intravenous drip was "usually preferable" to a full-dose intravenous injection or "push."[2] The plaintiff contended that the defendant should have strengthened its warning against intravenous push administration and the jury agreed, returning a verdict for the plaintiff.

On a post-trial motion for judgment as a matter of law, the defendant argued the plaintiff's claims were preempted by the FDCA. Under the statute, a drug may not be sold in interstate commerce unless an application which includes the drug's labeling has been approved by the FDA[3]; approval signifies the agency's determinations that the drug is safe for use under the conditions described in the labeling, and the labeling is not false or misleading in any particular.[4] After approval, the manufacturer must report all adverse drug experiences known to it to the FDA at least quarterly or, for serious and unexpected events, within 15 days.[5] If the agency determines, based on adverse event reports or otherwise, that new safety information should be included in the labeling, it has authority to require that.[6]

As noted, by the statute's own terms the manufacturer may not lawfully sell the drug with unapproved labeling[7] and such conduct could subject the manufacturer to seizure, injunctive relief, civil penalties or criminal prosecution.[8] Consistent with these provisions, therefore, the FDA's regulations generally require approval of a supplemental application before the manufacturer can implement labeling

changes. The regulations do contain a narrow exception, however — referred to as the "Changes Being Effected " or "CBE" regulation — under which the manufacturer can implement a change simultaneously with requesting approval, if based on "newly acquired information" it wishes to "add or strengthen a contraindication, warning, precaution, adverse reaction ... [or] instruction about dosage and administration ... intended to increase the safe use of the drug."[9]

In Wyeth, the defendant contended that the FDA's directive, in response to a prior request by defendant to modify the intravenous administration warnings, to "[r]etain verbiage in current label" represented the agency's prohibition of any strengthening of the intravenous push warnings.[10] The trial court rejected this argument, and the Vermont Supreme Court — treating preemption as a question of law requiring de novo review[11] — affirmed. The court held that the defendant's assertion of an FDA no-strengthening instruction, "[i]n other words, ... that [the FDA] would have rejected any attempt by the defendant to strengthen its label under the CBE regulations," was not supported by the record.[12] Among other things, the dialogue about the defendant's prior labeling proposal did not indicate the FDA's opinion of the value of intravenous push administration or that the FDA wished to preserve it, and the prior proposed warning, while different in discussing the dangers of that method, was not stronger or more prominent.[13]

After granting review, the United States Supreme Court also affirmed. Following discussion of the statutory and regulatory background, the court noted that "[o]f course, the FDA retains authority to reject labeling changes made pursuant to the CBE regulation, ... [b]ut absent clear evidence that the FDA would not have approved a change to Phenergan's label," the court would not reverse the no-preemption judgment.[14] Here, while the defendant had argued the regulatory record showed "the FDA intended to prohibit it from strengthening the warning about IV-push administration, ... both the trial court and the Vermont Supreme Court rejected this account as a matter of fact."[15] Accordingly, "[o]n the record before us, Wyeth has failed to demonstrate ... that [the FDA] would have prohibited" the warnings the plaintiff sought.[16]

Subsequently, many courts have interpreted Wyeth as affirmatively holding both that the burden in such a case is on the defendant to prove the FDA would have rejected the warning advocated by the plaintiff, and that the standard by which this must be shown is an "exacting" one beyond the normal preponderance-of-the-evidence standard. [17] In fact, neither proposition is correct. As to the first, the locus of any evidentiary burden of proof was not litigated by the parties, nor was it even discussed by any of the courts involved. As to the second, the standard for any such evidentiary burden was necessarily also not litigated or discussed.

Indeed, as to the second issue, Wyeth's "clear evidence" language was necessitated by the case's procedural posture. The court agreed the preemption issue was governed by how the FDA would have reacted to plaintiff's proposed label, but noted that both the Vermont trial and high courts had found against defendant "as a matter of fact." As the court would ordinarily not reverse the state courts' factual findings absent "exceptional circumstances,"[18] this explains the court's search for "clear evidence" in the defendant's favor and ultimate holding that the defendant had not demonstrated such evidence "[o]n the record before us."

In addition, the court's language may also have reflected prior precedent in which the court — at least in the context of so-called "obstacle" rather than "impossibility" preemption — articulated the need for a real, as opposed to speculative, conflict between state and federal law to establish preemption. For example, in Geier v. American Honda Motor Co., the court had noted that "a court should not find preemption too readily in the absence of clear evidence of a conflict,"[19] and other cases are to the same effect.[20]

At bottom, it is extraordinarily unlikely that the court was trying to articulate, even in dicta (because the issue was not litigated), an evidentiary burden of proof different from the longstanding preponderance-of-the-evidence standard with no discussion whatsoever. This is even more so where the court had previously, in considering the effect of statutory express preemption and savings clauses on implied conflict preemption arguments, expressly rejected the imposition of any "special burden" on such arguments, as this would only "complicat[e] well-established preemption principles that already are difficult to apply."[21]

Multiple Principles Place the Burden of Proof on the Plaintiff

Prescription drug failure-to-warn claims of the type asserted in Wyeth represent something of an anomaly in the application of implied conflict preemption principles. In the usual case, preemption is purely a legal question, asking whether the state law requirement at issue either directly conflicts with black-letter federal law or is an obstacle to accomplishing its purposes.[22] Thus no factual question is involved and any judicial interpretation of the congressional or administrative record leading to the purportedly preempting federal statute, rule or agency directive is considered merely that — legal interpretation.

Indeed, this would also be the case in prescription drug failure-to-warn cases under the terms of the FDCA itself, since it unambiguously forbids the manufacturer to use warnings not approved by the FDA.[23] It is only the CBE regulations — by purportedly authorizing the manufacturer under limited circumstances to make labeling changes while simultaneously submitting them for approval[24] — that

introduces a possible issue, as the legality of those changes then is determined by what the agency would eventually decide about them. Whether this question is a legal one, with the relevant agency record again being simply a matter for judicial interpretation, or a factual one, was not the subject of discussion in Wyeth and is beyond the scope of this article.[25]

If the question is treated as factual, however, it might be thought at first blush that since preemption is a "defense," the burden of proof on any factual issue that is at all relevant to the issue would necessarily be on defendant. As an initial matter, it is not clear that preemption principles are truly a "defense," much less an "affirmative" one, rather than simply part of the background law governing whether plaintiff may validly state a claim.[26] Regardless, there are multiple reasons why the burden should be on the plaintiff to prove the FDA would have approved the CBE proposal plaintiff claims defendant should have made, rather than on defendant to prove the agency would have rejected it.

First, given the undisputed background law that defendant could not lawfully have changed its warnings except by simultaneously submitting a CBE application, the essential gravamen of the plaintiff's claim is that the defendant should have submitted such an application and, necessarily, that the FDA ultimately would have approved it.[27] It is an unexceptional proposition that a plaintiff bears the burden of proving the essential elements of a plaintiff's claims.[28]

Viewed alternatively, in response to the plaintiff's claim that it should have warned differently, the defendant could assert as a "defense" that such a warning would be unlawful under the terms of the FDCA itself; the plaintiff would then in response rely on the purported exception to the FDCA's provisions created by the CBE regulation. It is an equally unexceptional proposition that the burden of proving the applicability of an exception to a statutory provision, or to any defense generally, lies on the party relying on the exception.[29]

Finally, federal objectives implicit in the FDCA require that the plaintiff bear the burden of proof. In Buckman v. Plaintiffs' Legal Commission the court held that state law fraud-on-the-FDA claims based on the defendant's application to market a medical device were impliedly preempted by the FDCA because it gave the FDA a range of remedies to police fraudulent submissions, "this authority is used by the agency to achieve a somewhat delicate balance of statutory objectives" and that balance "can be skewed" permitting the plaintiff's claims.[30] By the same token, the FDA's decision to approve a particular prescription drug and its labeling reflects a delicate balancing of objectives,[31] the agency has a range of options in the event adverse event reporting[32] leads it to believe the approved warning is no longer adequate, and permitting a lay jury to decide that a different warning should have been given when the agency did not exercise any of those options certainly risks "skewing" the agency's balancing decisions. Even if this does not mean that the plaintiff's claim is preempted by the mere fact of FDA approval, therefore, at the very least the plaintiff should bear the burden of showing the agency would have approved the different warning for which the plaintiff advocates.

Currently Pending Certiorari Petition

Interestingly, a currently pending certiorari petition, Johnson & Johnson v. Reckis, [33] raises issues under Wyeth but, as in that case, the state courts did not address any of the issues discussed in this article. Accordingly, the issue in Reckis appears to be only the narrow one of whether there was clear evidence the labeling change advocated by the plaintiff would have been rejected by the FDA when it was undisputed that the agency had actually rejected that change, but only as one of a proposed duo of rejected changes.

[1] Wyeth v. Levine, 555 U.S. 555, 571-72 (2009).

[2] Levine v. Wyeth, 183 Vt. 76, 83 n.1 (2006).

[3] 21 U.S.C. §§355(a), 355(b)(1)(F); 21 U.S.C. §331(d).

[4] 21 U.S.C. §355(d)(1)-(4), (7); 21 CFR §314.50(c)(2)(i).

[5] 21 CFR §314.80(b)-(c); see generally 21 U.S.C. §355(k)(1) (authorizing FDA to require reports of clinical experience with approved drugs).

[6] 21 U.S.C. §355(o)(4).

[7] See n. 4, above; unapproved labeling could also cause the drug to be unlawfully "misbranded" if the labeling were "false or misleading in any particular," 21 U.S.C. §352(a).

[8] 21 U.S.C. §332 (injunctive relief); 21 U.S.C. §333 (civil and criminal penalties); 21 U.S.C. §334 (seizure).

[9] 21 C.F.R. §314.70(c)(6)(iii)(A)-(C).

[10] Levine, 183 Vt. at 91.

[11] Id. at 84.

[12] Id. at 91-92.

[13] Id. at 92.

[14] Wyeth, 555 U.S. at 571.

[15] Id. at 572.

[16] Id. at 573.

[17] See, e.g. Forst v. SmithKline Beecham Corp., 639 F. Supp. 2d 948, 953-954 (E.D. Wis. 2009); see also Baumgardner v. Wyeth Pharms., Civil Action No. 05-5720, slip op. at 2 (E.D. Pa. Aug. 31, 2010) ("only if a defendant makes that showing [of clear evidence] will the plaintiffs' state-law tort claims be preempted"); Koho v. Forest Labs. Inc., 17 F. Supp. 1109, 1116 (W.D. Wash. 2014) ("to prevail on an impossibility conflict preemption claim, a defendant must provide clear evidence that the FDA would not have approved of a label change.")

[18] See, e.g., 324 Liquor Corp. v Duffy, 479 U.S. 335, 351 (1987) (Supreme Court "customarily accepts the factual findings of state courts in the absence of exceptional circumstances"); Cal. Retail Liquor Dealers Ass'n v. Midcal Aluminum, 445 U.S. 97, 111-112 ("we customarily accept the factual findings of state courts in the absence of 'exceptional circumstances'"); cf. Fed. R. Civ. P. 52(b) (findings of fact may not be set aside unless "clearly erroneous.")

[19] Geier v. Am. Honda Motor Co., 529 U.S. 861, 885 (2000) (emphasis added). Notably, however, the court did not rely on, or even quote, this language at any point in its decision in Wyeth, instead premising its holding on the Vermont courts' factual findings and the lack of clear evidence to reverse them.

[20] See, e.g., English v. General Elec. Co., 496 U.S. 72, 90 (1990) (rejecting conflict preemption where potential conflict was "too speculative"); Hillsborough County v. Automated Medical Laboratories Inc., 471 U.S. 707 at 720 (1985) (where the district court rejected appellee's factual assertions, concerns of conflict were "too speculative to support preemption.")

[21] Geier, 529 U.S. at 873.

[22] E.g., id. at 563-64 (citing Fidelity Fed. Sav. & Loan Assn. v. De la Cuesta, 458 U.S. 141, 153 (1982) and Hines v. Davidowitz, 212 U.S. 52, 67 (1941) for the respective implied conflict preemption sub-types).

[23] Under the statute itself, the only relevant "fact" would be what warning the agency had approved, which would be a matter of public record of which judicial notice could be taken.

[24] The validity of the CBE regulation is beyond the scope of this article. While the FDCA after its 2007 amendment, in authorizing the FDA to require labeling changes based on new safety information, refers to a "manufacturer's "responsibility ... to maintain its label in accordance with existing requirements, including ... [21 C.F.R] section 314.70," the statute does not refer specifically to the CBE regulation, which is only one small subpart of § 314.70, nor does that subpart appear to impose any "requirement" upon manufacturers.

[25] If the question is factual, of course, there could be a Seventh Amendment right to have it tried to a jury, an issue also beyond the scope of this article.

[26] Compare Wyeth, 555 U.S. at 573 (stating without citation or analysis that "preemption is a demanding defense" with International Longshoremen's Assoc. v. Davis, 476 U.S. 380, 385-93 (1986) (holding implied preemption of state tort claims under National Labor Relations Act not a waivable affirmative defense that had to be pled in answer or even raised at trial in order to be asserted in post-trial motion for judgment not withstanding verdict).

[27] If a proposed warning would ultimately be rejected by the FDA, the warning would not be a feasible one (save for during the temporary period when it was implemented but still awaiting agency action, which cannot be the proper measure of feasibility). While in most failure-to-warn cases the feasibility of the warning plaintiff advocates is not in question, feasibility is part of the plaintiff's burden of proving that the warning given was defective. See, e..g., Humble Sand & Gravel v. Gomez, 146 S.W. 3d 170, 189-90 (Tex. 2004); Restatement (Third) of Torts: Product Liability, § 2 cmt. i (AM. LAW INST. 1998) (if there is reason to doubt employer will pass manufacturer's product warning on to employees, manufacturer must warn employees directly "if doing so is reasonably feasible.")

[28] Schaffer v. Weast, 546 U.S. 49, 56-57 (2005); Lujan v. Defenders of Wildlife, 504 U.S. 555, 561 (1992); Cleveland v. Policy Management Systems Corp., 526 U.S. 795, 806 (1999); Hunt v. Cromartie, 526 U.S. 541, 553 (1999).

[29] United States v. First City Nat'l Bank, 386 U.S. 361, 366 (1967) (citing 2A C. Sands, Sutherland on Statutory Construction § 47.11, p. 90 (4th ed. 1973) (party "who claims the benefit of an exception from the prohibition of a statute has the burden of proving that his claim comes within the exception")); see also Waters v. ShopRite Supermarkets Inc., 2:10-cv-02986, slip op. at 6 (D N.J. Dec. 5, 2011) (in claim under Age Discrimination in Employment Act, "Plaintiffs argument conflates two burdens of proof:; the burden of proving an

affirmative defense and the burden of proving an exception to an affirmative defense. Plaintiff is correct that a defendant bears the burden of proving an affirmative defense. ... Plaintiff is not correct that a defendant bears the burden of proving the exception to an affirmative defense; that burden falls on plaintiff.")

[30] Buckman Co. v. Plaintiffs' Legal Comm., 531 U.S. 341, 348 (2001).

[31]United States v. Rutherford, 442 U.S. 544, 555 (1979) ("Few if any drugs are completely safe in the sense that they may be taken by all persons in all circumstances without risk. Thus, the [FDA] generally considers a drug safe when the expected therapeutic gain justifies the risk entailed by its use."); FDA v. Brown & Williamson Tobacco Corp., 529 U.S. 120, (2000) ("the product's probable therapeutic benefits must outweigh its risk of harm.")

[32] The FDA would have the benefit of adverse event reporting not only by the defendant but every manufacturer of the same compound, every manufacturer of other drugs in the same therapeutic class and every manufacturer of drugs in other classes that also pose the same risk.

[33] Johnson & Johnson v. Reckis, 471 Mass. 272 (2015), petition for cert filed, (U.S. Oct. 8, 2015) (No. 15-449).

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